REMARKS

This Response is filed in connection with the Office Action mailed September 8, 2004. Claims 1 to 39 and 41 to 65, 71 and 72 are pending. Claims 1 to 39 and 41 to 64 stand withdrawn from consideration as directed to a non-elected invention. Accordingly, claims 65, 71 and 72 are under consideration.

Applicants thank the Examiner for the interview held August 18, 2004. The claim amendments and remarks herein address all rejections of record, as discussed in the interview.

Regarding the Amendments

The amendments to claims 65, 71 and 72 are supported throughout the specification or were made to address various informalities. In particular, the amendment to claim 65 was made in response to the Examiner's request for this specific language, and was made for reasons unrelated to patentability since the meaning and scope of claim 65, prior to and after entry of the amendment, is the same. The amendments to claim 71 to recite that "binding of" the anti-MAFA antibody or the antigen binding "fragment thereof to the MAFA expressed on the NK or T cells" generates an inhibitory signal to the NK or T cell "thereby inhibiting" an activity of the NK or T cell is supported, for example, at page 4, lines 19-25, which discloses that an agent that specifically binds to an NK or T cell expressed cell surface MAFA can generate an inhibitory signal to the NK or T cell, which can prevent or inhibit an NK or T cell activity, such as a decrease in NK cell or T cell mediated cell killing. This amendment to claim 71 is also supported, for example, at page 7, lines 6-12, which discloses that a method for inhibiting an activity of an NK or T cell includes providing an antibody or subsequence of an anti-MAFA antibody which is administered in an amount sufficient to inhibit an activity of the NK or T cell, which in one embodiment, is cell killing by the NK cell or the T cell (see, also, page 10, lines 1-12; page 31, lines 5-18; and page 32, lines 1-6). The amendment to claim 72 was made in order to define the claimed subject matter with greater particularity. Thus, as the amendments to the claims are supported by the specification or were made to address various informalities, no new matter has been added and entry thereof is respectfully requested.

I. OBJECTION TO THE DISCLOSURE

The Examiner has acknowledged Applicants' request to hold the objection to the specification for grounds relating to the ATCC deposit in abeyance until notification of allowable subject matter. Applicants thank the Examiner for holding the objection in abeyance.

II. REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The rejection of claims 65, 71 and 72 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement is respectfully traversed. The grounds for rejection are of record.

The specification enables claims 65, 71 and 72 prior to the present amendment. Nevertheless, solely in order to further prosecution of the subject application and without acquiescing to the propriety of the rejection, claims 65, 71 and 72 have been amended as set forth above. The rejection will therefore be addressed as it may pertain to the amended claims.

The specification adequately enables claims 65, 71 and 72, as amended. Applicants respectfully point out that the specification discloses antibodies that inhibit ligand binding to NK or T cell expressed MAFA. For example, the specification discloses that pharmaceutical agents, which include antibodies (page 4, lines 1-4; see, also, page 10, lines 13-17, and page 13, lines 11-13) that bind to NK or T cell expressed cell surface MAFA can prevent or inhibit NK or T cell surface-expressed MAFA from binding to a MAFA ligand (page 3, lines 14-17; see, also, page 5, line 26, to page 6, line 5). The specification exemplifies such anti-MAFA antibodies (e.g., 7B51 and F10) that bind to MAFA, that inhibit MAFA from binding to a MAFA ligand, and that generate an inhibitory signal to the NK or the T cell that in turn inhibits an activity of the NK or the T cells (see, for example, page 7, lines 6-12; page 10, lines 20-21; and page 31, line 11, to page 32, line 5). The specification additionally discloses that, although not limited to a particular functional mechanism, the compositions and methods of the invention can be used to inhibit or block NK cell and T cell activities by mimicking the binding of a cell surface expressed MAFA polypeptide interaction with a ligand expressed on a target cell, and that methods of the invention can be used to inhibit NK cell and T cell activities by initiating or augmenting or stimulating the ability of cell surface expressed MAFA to transmit inhibitory signals to these cells (page 10, lines 1-17). Thus, in view of the specification, the skilled artisan would know anti-MAFA antibodies that bind to MAFA expressed on NK or T cells that inhibit

ligand binding to NK or T cell expressed MAFA, and antibodies which generate an inhibitory signal to the NK or T cell thereby inhibiting an activity of an NK or T cell.

Furthermore, the specification teaches how to produce polyclonal and monoclonal antibodies, including anti-MAFA antibodies that bind to MAFA expressed on NK or T cells that inhibit ligand binding to NK or T cell expressed MAFA, and antibodies that generate an inhibitory signal to the NK or T cell thereby inhibiting an activity of an NK or T cell, using routine methods known in the art at the time of the invention (see, for example, page 22, line 16 to page 23, line 12; page 26, line 24, to page 28, line 11; and page 28, line 21, to page 29, line 11, and the references cited therein). Modified antibodies (e.g., having substitutions, deletions and additions) can readily be produced, in view of the knowledge of antibody structure and function in the art at the time of the invention. Further in this regard, methods for producing antibodies having amino acid substitutions, deletions and additions, mimetics, and humanized forms are disclosed in the specification, and such methods were also routine in the art at the time of the invention (see, for example, page 11, line 13, to page 12, line 15; page 13, line 11, to page 15, line 11; and page 21, lines 8-21, and the references cited therein). Assays for identifying anti-MAFA antibodies having the requisite activity are disclosed in the specification. For example, the specification discloses assays for measuring cytotoxic activity of NK and CTL cells, which were routine in the art at the time of the invention (see, for example, page 28, lines 12-19; page 29, line 20, to page 30, line 7, and the references cited therein). Thus, in view of the guidance in the specification and of knowledge in the art at the time of the invention, the skilled artisan could readily produce and identify anti-MAFA antibodies that bind to MAFA expressed on NK or T cells that inhibit ligand binding to NK or T cell expressed MAFA, and anti-MAFA antibodies that generate an inhibitory signal to the NK or T cell thereby inhibiting an activity of an NK or T cell, including modified forms, without undue experimentation.

The specification exemplifies two particular anti-MAFA antibodies, 1F10 and 7B5 (page 28, line 21 to page 29, line 19), each of which bind to MAFA expressed on NK or T cells, that inhibit ligand binding to NK or T cell expressed MAFA, and that generate an inhibitory signal to the NK or T cell thereby inhibiting an activity of an NK or T cell (page 29, line 20, to page 30, line 7; see, also, page 31, lines 4-18). The fact that such anti-MAFA antibodies were produced without undue experimentation corroborates that anti-MAFA antibodies that bind to MAFA expressed on NK or T cells, that inhibit ligand binding to NK or T cell expressed MAFA,

and that generate an inhibitory signal to the NK or T cell thereby inhibiting an activity of an NK or T cell, in general, can be produced without undue experimentation, in view of the guidance in the specification. Consequently, as undue experimentation would not be required to obtain such anti-MAFA antibodies, claims 65, 71 and 72 are adequately enabled.

Finally, as previously pointed out the cited Kuby *et al.*, Ngo *et al.* and Abaza *et al.* references are irrelevant to enablement of claims 65, 71 and 72. In this regard, Kuby *et al.*, Ngo *et al.* and Abaza *et al.* describe the effect of *antigen* alterations on immunogenicity. However, the skilled artisan need not alter MAFA antigen in order to produce additional anti-MAFA antibodies and modified forms that bind to MAFA expressed on NK or T cells, that inhibit ligand binding to NK or T cell expressed MAFA, and that generate an inhibitory signal to the NK or T cell thereby inhibiting an activity of an NK or T cell. As discussed above and in the record, additional anti-MAFA antibodies can be produced and identified without undue experimentation without having to alter MAFA antigen. Thus, the skilled artisan would not need to know how altering MAFA affects immunogenicity in order to obtain additional anti-MAFA antibodies. Consequently, as additional anti-MAFA antibodies having the requisite activity can be produced and identified without altering MAFA antigen, Kuby *et al.*, Ngo *et al.* and Abaza *et al.* are irrelevant to enablement of claims 65, 71 and 72.

The anti-MAFA antibodies recited in the claims of the subject application is analogous to *In re Wands* in that "there was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." *In re Wands,* 858 F.2d 731, 737 (Fed. Cir. 1988). The court concluded that undue experimentation would not be required to obtain antibodies needed to practice the claimed invention. Here as in *Wands*, the level of skill in the art is high and methods for producing anti-MAFA antibodies are taught by the specification or were known in the art at the time of the invention. Accordingly, as in *Wands*, undue experimentation would not be required to obtain additional anti-MAFA antibodies, and as such, claims 65, 71 and 72 are adequately enabled.

In view of the foregoing, claims 65, 71 and 72 are adequately enabled. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

The rejection of claim 72 under 35 U.S.C. §112, first paragraph, as allegedly lacking an adequate written description, is respectfully traversed. The grounds for rejection are due to alleged new matter.

An adequate written description for claim 72, prior to the entry of the amendment, is provided. Nevertheless, solely in order to further prosecution of the subject application and without acquiescing to the propriety of the rejection, claim 72 has been amended as set forth above.

Claim 72, prior to entry of the amendment, recites that the activity inhibited comprises "secretion of a cytokine." The specification discloses that anti-MAFA antibodies of the invention can be used to manipulate NK and T cell activities (see, for example, page 22, lines 11-15). For example, the specification discloses anti-MAFA antibodies that inhibit cytotoxic activity of NK and T cells (see, for example, page 10, lines 20-21; and page 30, lines 1-4; and page 32, lines 1-3). The specification also discloses that an activity of NK or T cell is cytokine secretion (see, for example, page 3, lines 26-28; page 4, lines 13-17 and lines 25-26; and page 6, lines 23-24). Thus, in view of the foregoing, the specification adequately describes anti-MAFA antibodies that inhibit NK cell- or T cell-mediated secretion of a cytokine. Consequently, an adequate written description for the subject matter of claim 72, prior to the amendment, is provided. As such, the rejection based upon alleged new matter is improper and must be withdrawn.

Nevertheless, solely in order to further prosecution of the subject application and without acquiescing to the propriety of the rejection, claim 72 has been amended as set forth above to delete reference to secretion of a cytokine. Accordingly, the ground for rejection is moot and Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph, as allegedly lacking an adequate written description.

III. REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The rejection of claims 65, 71 and 72 under 35 U.S.C. §112, second paragraph, as allegedly indefinite is respectfully traversed. The grounds for rejection are based upon particular claim terminology.

Claim 65 has been amended as suggested by the Examiner. Claim 71 has also been amended to delete reference to "agonist." These amendments were made solely in order to

further prosecution of the application, do not alter the meaning or scope of claims 65 and 71, and were made without acquiescing to the propriety of the rejection.

As to the remaining amendments suggested, Applicants respectfully remind the Patent Office of the proper standard for complying with 35 U.S.C. §112, second paragraph. In this regard, Applicants respectfully direct the Examiner's attention to M.P.E.P. §2173.02, particularly, the section that reads "[t]he examiner's focus during examination of claims for compliance with....35 U.S.C. §112, second paragraph is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available." [Emphasis added] Furthermore, "latitude in the manner of expression and the aptness of terms should be permitted." The determining factor is "whether the claim apprises one of ordinary skill in the art of its scope." *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379 (Fed. Cir. 2000) By this standard, the meaning of claim 72 would be clear and definite to the skilled artisan.

As to claim 71 and the suggested amendments, it appears that the Examiner has misunderstood the activity of the specifically recited anti-MAFA antibodies. In particular, the assertion that "[t]he agonist antibody does not generate an inhibitory signal to the NK or T cells," is incorrect. MAFA is an inhibitory receptor and binding to MAFA ligand transmits an inhibitory signal that inhibits an NK or T cell activity (see, for example, page 10, lines 1-17). As discussed above, the specification discloses and exemplifies anti-MAFA antibodies that mimic MAFA ligand, and that generate an inhibitory signal that inhibits an NK or T cell activity (see, for example, page 4, lines 19-25; page 10, lines 1-12; and page 31, lines 5-18; and page 32, lines 1-5). Claim 71 has therefore been amended to be consistent with the function of the recited MAFA-antibodies, namely that "binding of the anti-MAFA antibody or the fragment thereof to the MAFA expressed on the NK or T cells generates an inhibitory signal to the NK or the T cell that inhibits an activity of the NK or the T cell." In view of the amendment and the specification, the meaning of claim 71 would be clear and definite to the skilled artisan.

In view of the amendments and foregoing remarks, claims 65, 71 and 72 are clear and definite. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

CONCLUSION

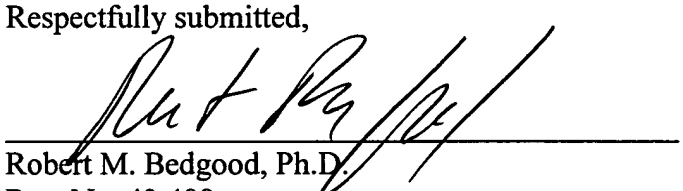
In summary, for the reasons set forth herein, Applicants maintain that claims 65, 71 and 72 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 509-4065.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-2212.

Respectfully submitted,

Date: 2-23-05



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